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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,039	07/12/2001	Shoulian Dong	3218.2A	3123

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AFFYMETRIX, INC
ATTN: CHIEF IP COUNSEL, LEGAL DEPT.
3380 CENTRAL EXPRESSWAY
SANTA CLARA, CA 95051

EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/904,039	Applicant(s) DONG ET AL.	
	Examiner Young J. Kim	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-173* is/are pending in the application.

4a) Of the above claim(s) *38 and 59-173* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action responds the Amendment received on February 19, 2003 (Paper No. 13).

Preliminary Remark

Claims 38 and 59-173 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 39-58 are under prosecution therefore.

Claim Rejections - 35 USC § 112

The rejection of claims 39-58 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on November 19, 2002 is withdrawn in view of the Amendment received on February 19, 2003, amending the independent claim 39.

Claim Rejections - 35 USC § 101

The rejection of claims 39-58 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-8, 11-15, and 18-24 of prior U.S. Patent No. 6,361,947 B1, made in the Office Action mailed on November 19, 2002 is withdrawn in view of careful reconsideration and also in view of the arguments presented in the Amendment received on February 19, 2003.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 39-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-15, and 18-24 of U.S. Patent No. 6,361,947 B1. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claims are not patentably distinct from the reference claims because the examined claims are anticipated by the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ 2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ 2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.3d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of the '947 patent recites several embodiments of practicing its method in a Markush language while claim 39 of the instant application is drawn to the one of the embodiments of the Markush member iterated in the '947 patent, rendering the claims anticipated though different in their scope. The dependent claims thereon; claims 2-8, 11-15, and 18-24 of the '947 patent and claims 40-58 are verbatim as illustrated below:

Instant Application	U.S. Patent No. 6,361,947 B1

Claims 40-46	Claims 2-8
Claims 47-51	Claims 11-15
Claims 53-58	Claims 18-24

Claim Rejections - 35 USC § 102 – Necessitated by IDS

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39, 44, 45, and 48-55 are rejected under 35 U.S.C. 102(e) as being anticipated by McCaskey Feazel et al. (U.S. Patent No. 6,100,030, issued August 8, 2000, priority January 10, 1997).

Claim 39 is drawn to a method of analyzing a first nucleic acid sample by fragmenting the first nucleic acid, ligating adaptors sequences to the resulting fragments, amplifying the ligated fragments and hybridizing the resulting amplified ligated fragments to a nucleic acid array and analyzing their hybridization pattern.

The method is also drawn to detecting a sequence variation in the nucleic acid (claim 52), wherein the variation is a single nucleotide polymorphism (SNP) (claim 53).

The method requires that the nucleic acids on the nucleic acid array hybridizes to the amplified ligated fragments (claims 54-55).

Some embodiments are drawn to the first nucleic acid being a DNA (claim 44), genomic DNA (claim 45).

Some embodiments are drawn to the nature of the fragmentation produced by a restriction enzyme (claim 48), a type IIs endonuclecase (claim 49).

Some embodiments are drawn to the nature of the adaptor sequence (claims 50 and 51).

McCaskey Feazel et al., hereto referred to as '030 patent, disclose a method for detecting polymorphism (column 23, line 40; column 22, lines 33-37; claim limitation 52 and 53) in a nucleic acid sample by fragmenting genomic DNA (column 18, lines 20-21; claim limitation 44 and 45), ligating adaptor sequences to the resulting fragments (column 18, lines 24-25), wherein the adaptor sequences are complementary to the PCR primer sequences (column 18, lines 25-29 and 60-63, claim limitation 50-51), amplifying the adapter litgated fragments and hybridizing them to a microarray comprising an array of nucleic acids which are complementary to the amplified, adapter ligated fragments (column 23, lines 54-60, claim limitation 54-55). The method of the '030 patent employs a restriction endonuclease (column 18, line 21, claim limitation 48 and 49) for producing the nucleic acid fragments. The '030 patent discloses that any type of restriction endonucleases known in the art can be used to digest the DNA for its analysis (column 18, line 36-38).

Therefore, McCaskey Feazel et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103 – Necessitated by IDS

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 40-43, 46, 47, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCaskey Feazel et al. (U.S. Patent No. 6,100,030, issued August 8, 2000, priority January 10, 1997) in light of DeRisi et al. (Science, October 1997, vol. 278, pages 680-686).

McCaskey Feazel et al., hereto referred to as '030 patent, disclose a method for detecting polymorphism (column 23, line 40; column 22, lines 33-37) in a nucleic acid sample by fragmenting genomic DNA (column 18, lines 20-21), ligating adaptor sequences to the resulting fragments (column 18, lines 24-25), wherein the adaptor sequences are complementary to the PCR primer sequences (column 18, lines 25-29 and 60-63), amplifying the adapter litgated fragments and hybridizing them to a microarray comprising an array of nucleic acids which are complementary to the amplified, adapter ligated fragments (column 23, lines 54-60). The method of the '030 patent employs a restriction endonuclease (column 18, line 21) for producing the nucleic acid fragments. The '030 patent discloses that any type of restriction endonucleases known in the art can be used to digest the DNA for its analysis (column 18, line 36-38).

McCaskey Feazel et al. do not teach the amplified, adapter ligated nucleic acids (or second nucleic acids) comprising various lengths (by percentage) of the initial DNA (claims 40-43), nor do the artisans disclose the DNA being a cDNA produced from an RNA molecule (claim 46). McCaskey Feazel et al. also do not *explicitly* teach a method of determining the sequence of the probes of the microarray by a computer system.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of McCaskey Feazel et al. with the conventional knowledge in the art to arrive at the invention as claimed for the following reasons.

Although McCaskey Feazel et al. do not explicitly teach that the amplified, adapter ligated nucleic acid (or second nucleic acids) comprising various lengths (by percentage), artisans clearly envision producing fragments of various lengths because the artisans clearly state that all different types of restriction endonucleases could be used in their method. It is an art recognized knowledge that different restriction endonucleases cut at different sequences producing fragments of various lengths.

With regard to the determination of the probe sequence by a computer, such knowledge is also demonstrated by McCaskey Feazel et al. because the artisans make reference to Affymetrix™, DNA VLSIP™ arrays (column 24, lines 35-50), wherein the probes tiled therein are predetermined via computer. The artisans also state that the probe lengths could be altered to allow maximum specificity with their targets (or second nucleic acids), the method of which are conducted on a computer system.

Finally, although McCaskey Feazel et al. do not use cDNAs produced from RNAs (claim limitation 46) for fragmentation, such knowledge, as demonstrated by DeRisi et al., is also within the purview of an ordinarily skilled artisan in the field of array hybridization. The advantage (or motivation) to use the cDNA as a starting material is demonstrated by DeRisi et al.:

"[v]irtually all differences in cell type of state are correlated with changes in the mRNA levels of many genes. This is fortuitous because the only specific reagent require to measure the abundance of the mRNA for a specific gene is a cDNA sequence." (page 680, 1st column)

The cDNA is disclosed as being derived from mRNA by reverse transcription process and hybridized to a DNA array (page 680, 3rd column).

Therefore, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in substituting the genomic DNA of McCaskey Feazel et al. with cDNA of DeRisi et al. because both types of DNAs were demonstrated to be hybridizable to DNA arrays.

Therefore, the invention as claimed is obvious over the cited references.

Conclusion

Claims 57 and 58 are free of prior art as the prior art do not teach or suggest the method of mixing a probe-bead complex to isolate a polymorphic sequence with a first nucleic acid population, followed by their exposure to a DNA nuclease to digest the unbound nucleic acid (*i.e.,* single stranded), followed by ligation of the remaining double-stranded molecules with double stranded adapters comprising a restriction site, followed by their digestion with a endonuclease to separate the beads from the adapter ligated double stranded nucleic acid for their SNP analysis on a microarray.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so

as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

3/20/03

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/27/03

John J. Doll, Director
Technology Center 1600